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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/595,161	03/10/2006	Mark Jozef Albert Waer	50304/114001	3570
21559	7590	02/12/2008		
CLARK & ELBING LLP 101 FEDERAL STREET BOSTON, MA 02110			EXAMINER HUGHES, ALICIA R	
			ART UNIT	PAPER NUMBER
			1614	
			NOTIFICATION DATE	DELIVERY MODE
			02/12/2008	ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/595,161	<b>Applicant(s)</b> WAER ET AL.	
	<b>Examiner</b> Alicia R. Hughes	<b>Art Unit</b> 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 10 March 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 8-27 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 8-27 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 10 March 2006 is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>7 sheets</u> . | 6) <input type="checkbox"/> Other: _____  |

## DETAILED ACTION

### *Status of the Claims and Examination*

Claims 8-27 are pending and the subject of this Office Action.

### *Claim Rejections - 35 U.S.C. §112.1*

The following is a quotation of the first paragraph of 35 U.S.C. §112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 8 is enabled for the treatment of the toxic effects of TNF- $\alpha$ , alcohol-induced hepatitis, and cachexia by administering a compound of the instant invention. However, the claimed prophylaxis of the toxic effects of TNF- $\alpha$ , alcohol-induced hepatitis, and cachexia is not supported by the specification. As a result, the effect of performing the invention by one skilled in the art would be that of undue experimentation.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The

factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in organic chemistry is high, the results of experiments to discover treatments for the illnesses and conditions recited in claim 8, is unpredictable. While all of the Wands factors are considered, a sufficient amount for a *prima facie* case is discussed below.

The applicant has provided a number of working examples for treating patients with disorders in claim 8. However, the applicant has failed to enable the prevention of these disorders. Prophylaxis is generally defined as "the preventing of disease." Random House Unabridged Dictionary, Random House, Inc. 2006. While there is support for the treatment of the toxic effects of TNF- $\alpha$ , alcohol-induced hepatitis, and cachexia, the specification is void of support for the prevention of the same.

As such, the art of the claimed invention lacks predictability because the claim as written to include prevention of interstitial cystitis is drawn too broadly.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 8-27 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 31 of U.S. Patent Application No. 10-557,541. Although the conflicting claims are not identical, they are not patentably distinct from each other because the '541 patent application, like the instant invention, is drawn to a method of treating or

preventing a pathologic disease or disorder. The methods articulated in claim 31 of the '541 application overlap in scope with the methods articulated in claims 8-27 of the instant invention, because both utilize compounds with an identical core structure to treat the same family of disease, cachexia in one instant, which is a known effect of cancer and a cell proliferative disorder, of which cancer is known to be one.

This is a provisional rejection, because the claims have not, in fact, been patented.

In looking in continuity data, it is noted that applicant has numerous pending applications encompassing the same or similar subject matter of the instant application. Applicant should review all subject matter considered the same or similar, and submit the appropriate Terminal Disclaimer(s). For example, pending patent applications with the same or similar subject matter include, but are not limited to 10/595,126 and 11/402423.

### ***Claim Rejections – 35 U.S.C. §102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

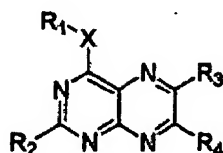
A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 8-27 are rejected under 35 U.S.C. §102(a) and §102(e) as being anticipated clearly by U.S. Patent Publication No. 2004/0077859 A1 [hereinafter referred to as "Waer et al"] (Please consider the reference in its entirety).

Waer et al disclose novel pteridine compounds, with the core structure of



wherein X can represent an oxygen atom or a group with the formula NZ; Z is a group independently defined as R1 or Z is hydrogen or the group NZ together with R1 is either hydroxylamino or an optionally substituted heterocyclic group containing at least one nitrogen atom; R3 together with R4 forms a homocyclic or heterocyclic radical (Pages 4 to 5, para. 23); and R4 can be hydrogen, halogen, etc (Page 3, para. 22).

Waer et al also teach pharmaceutically acceptable addition salts stereoisomers and dihydro or tetrahydropteridine derivatives of the above structure (Page 5, para. 24). These compounds can be used to treat or prevent hepatitis B-, C-, and D- (Page 18, paras 149-153 and 155). A specific example of a compound representative of the above formula is 2-amino-4-piperazino-6-(4-methoxyphenyl) pteridine (Page 22, para. 218).

In view of the foregoing, claims 8-27 are clearly anticipated by Waer et al.

#### ***Claim Rejections – 35 U.S.C. §103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

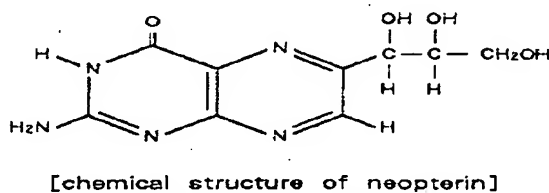
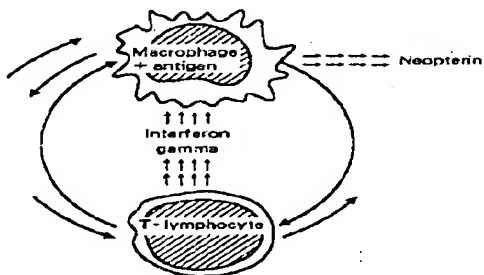
This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 8-27 are rejected under 35 U.S.C. 103(a) as being obvious over Iwagaki, H., et al, "Decreased Serum Tryptophan In Patients With Cancer Cachexia Correlates With Increased Serum Neopterin," *Immunological Investigations*, Vol. 24, Issue 3, pages 467-478 (1995)[Iwagaki, et al"] (Please consider the reference in its entirety.

Iwagaki et al disclose the following chemical structure for neopterin

TRP IN PATIENTS WITH CANCER CACHEXIA

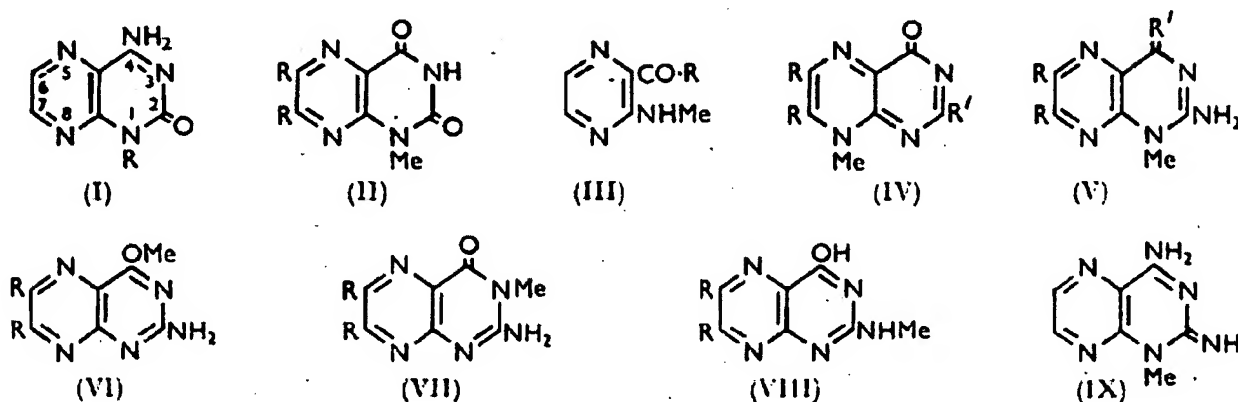
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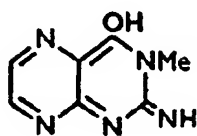


and teaches that neopterin [hereinafter referred to as "NPT"] comes from activated macrophages that are activated by tumor-sensitized T cells via gamma interferon (IFN- $\gamma$ ) (See Abstract; Page

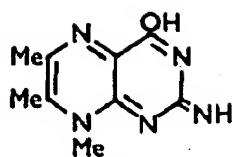
468, lines 14-20) and that NPT is released from cells based on the interaction of T-cells and macrophages (Page 469, Figure 2). Iwagaki et al also teach that an increase in NPT production and presence in tumor cells is indicative of cancer cachexia (Page 468, lines 20-26; Page 471, lines 1-3; Page 473, lines 7-13), and that presence of NPT has an inverse relationship with the presence of tryptophan (Page 473, lines 7-13). Thus, an increase in the levels of tryptophan would reflect a decrease in the levels of NPT, thereby effectively treating and potentially preventing cachexia. (Page 476, Figure 5 and text thereafter).

NPT is an obvious variation of the core structure of the instant invention, differing mainly by the functional group attached NPT's position one and the position of the oxygen substituent at position four rather than, for example, a methyl ether, as contemplated by the instant invention. Based on the examples below, as disclosed in Brown, D.J., et al, "Pteridine Studies. Part XIV. Methylation of 2-Amino-4-hydroxypteridine and Related Compounds," *J. Amer. Chem. Soc.*, Vol. 869, pages 4413-4420 (1961), as early as 1961 this core structure was known and with varying substitutions, such as oxygen, hydroxyl, methyl, amines, and methyl

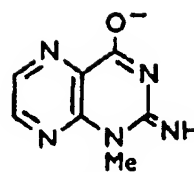




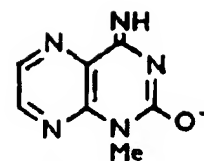
(X)



(XI)



(XII)



(XIII)

ether, at various positions on the ring in question. For example, structure 12 above shows the core structure with a reactive oxygen site for which the methyl group could easily attach to stabilize the compound, which would yield the compound of the instant invention. The suggestion therefore, is that these reactive sites are not necessarily critical for to functionality of the compound as a whole.

In light of the foregoing, it would have been *prima facie* obvious to one of ordinary skill modify the teachings of Iwagaki et al by substituting the compound of the instant invention and concluding that the same would be useful in the treatment of cachexia.

### Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alicia Hughes whose telephone number is 571-272-6026. The examiner can normally be reached from 9:00 A.M. until 5:00 P.M. on Monday through Friday.

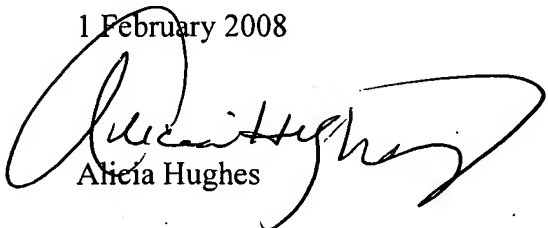
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached at 571-272-0718. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

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1 February 2008



Alicia Hughes



RAYMOND HENLEY III  
PRIMARY EXAMINER  
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